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Experimental Studies on the Impact of Deficient Diet on Behavior

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1. INTRODUCTION

The relations between food and behavior may be examined in reference to two types of problems: First, the behavior of man toward food and, second, the impact of food on behavior.[1] In the first category, we deal with the phenomena of food appraisal and food consumption: with hunger and thirst;[2] taste, flavor and food acceptance;[3] and gross deviations from the physiological caloric requirements, with a positive balance leading, over a period of time, to obesity[4] and the negative balance resulting in emaciation, typified by a patient in an advanced stage of anorexia nervosa.

The present survey is limited to topics in the second category, with decided emphasis on experimental studies in which quantitative methods for the study of human behavior under conditions of nutritional deficiency have been used. This accounts for the concentration in this review on studies carried out at the Laboratory of Physiological Hygiene, University of Minnesota.

2. METHODS FOR LABORATORY STUDY OF HUMAN BEHAVIOR

In fundamental investigations of the biological effects of nutritional deficiencies the coverage of the behavioral aspects should be as comprehensive as the time and facilities permit. The principal procedures used in nutritional studies carried out at the University of Minnesota were described.[5a] The tests and procedures were grouped into 4 categories: Special Senses, Motor Performance (strength, speed, and coordination), Intelligence ("mental level", timed tests of intellective performance, tests of learning ability), and Personality (interviews, diaries, questionnaires, ratings). Some of these tests and procedures were used in all the nutritional experiments carried out at the University of Minnesota. Additional methods were used. They were described in reports of separate studies or in special communications devoted to problems of methodology.

Within the framework of each study, the procedures were rigorously standardized. Whenever possible, methods described in the literature and available on the market were used. From this point of view the situation was most satisfactory as regards intelligence and personality. It was less satisfactory in reference

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to special senses and still less so in regard to motor performance. The tests of motor functions used in the nutritional research at the University of Minnesota were described.[6] Nutritional studies involve, typically, measurements made at intervals of days, weeks and months. For such purposes a battery of six short tests of intellective performance was assembled. The work-time allotments, principles underlying the construction of a large number of alternative forms of each test, their reliabilities, and effects of learning were presented.[7]

The methodological problems encountered in measuring performance capacity under conditions of laboratory studies on human nutrition, with emphasis on nutritional stresses, were discussed in detail.[8a] Reference was made also to real-life situations, principally industrial studies, and to miniature work situations which were a cross between industrial operations and laboratory performance tests. Such a synthetic work test, reproducing industrial inspection, was used in an exploratory study on the effects on the composition of a noon meal.[9] In view of the difficulties inherent in research on industrial nutrition, the simplified replicas of actual industrial (or military) operations may deserve greater attention than they received in the past.

3. ACUTE STARVATION

Acute starvation is defined as the total absence of food, with free access to water.

Around the turn of the century, various "hunger artists" underwent prolonged fasts, with surprisingly unimpressive signs of deterioration in psychological functions.[10] By contrast to these men who kept their energy expenditure at a low level, marked changes in some aspects of performance capacity and feeling of well being were found in normal young men undergoing four days of starvation combined with hard physical work.[11] In regard to manipulative performance, there was a statistically highly significant deterioration in tests of speed and coordination. The speed of simple repetitive movements (two-plate tapping) and of more complex, coordinated movements, including hand and arm, was substantially reduced. There was a marked increase in the complex reaction time to visual stimuli. Body sway, measured with the eyes closed, increased. Marked deterioration was present in the test of eye-hand coordination.[12] Interestingly enough, there was no decrement in hand grip, and the decrement in back-pull (lift strength) was negligible. The principal subjective symptoms and complaints included tiredness, weakness (not reflected in strength measurements), and decreased ability to concentrate. The men felt sleepy and their self-initiated activities decreased. Nausea was a common complaint, especially after runs on the treadmill used to measure the changes in cardiovascular functions under the stress of severe physical work and as measures of endurance. In spite of the availability of water, the men complained of dryness of the throat.

Metabolically, the alterations that may account for the initial changes in nervous and motor functions include lowered blood sugar, ketosis and dehydration.[13] In advanced diabetes with acidosis and ketosis a profound (40%) reduc-

tion in cerebral utilization of oxygen in the presence of undiminished cerebral blood flow and a normal arterial oxygen saturation was reported.[14] The accumulation of ketone bodies in the blood of individuals in the advanced state of acute starvation may lead to severe disturbances of cerebral metabolism and function.

4. SHORT-TERM CALORIC DEFICIT

Within the investigations related to the development of all-purpose survival rations, a series of experiments was carried out on potential changes in performance capacity resulting from maintenance on restricted intakes of food and, later, also of water. These studies represented a continuation of the earlier work on the impact of nutritional deficits on the human organism, some of which are described in the preceding and in the two following sections of this review.

In the control period the subjects were given a mixed diet (Army C rations), with an actual food intake of 3,280 cal/day. During the 24 days of dietary restriction the only carbohydrate given was in the form of jelly bars and a carbonated soft drink. Adequate supplements of salt (4.5 gm NaCl/day) and vitamins were provided. Black coffee was limited to six cups per day. Water was allowed *ad libitum*. The average daily energy deficit was about 1,600 to 1,700 calories.

The effects of maintenance on this low-calorie carbohydrate diet were examined in reference to selected morphological,[15] physiological,[16] and psychological[17] characteristics.

The total mean weight loss was moderate, amounting to 7.6 kg or approximately 11% of the initial body weight. Measurements of visual functions and hearing revealed no deterioration. This is in line with the expectations and previous experience. The caloric deficit was only moderate and there are no theoretical indications that elimination of fat and protein from the diet would result in a deterioration of sensory functions. In general, the sensory functions, except for deterioration in dark adaptation as a specific response to prolonged and severe vitamin A deprivation, have shown remarkable resistance to nutritional stresses studied under rigorously controlled conditions in the laboratory. At the same time, clinical experience with complex (vitamin) deficiencies, at times perhaps combined with the presence of toxic agents in the diet, has provided ample documentation for impairment of the senses of vision and hearing,[18] dietary in origin.

The motor facet of fitness received major attention in the experiment on low-calorie carbohydrate diet. In addition to grip strength, measured by the standard hand grip dynamometer, the speed of single ballistic leg movements,[19] speed in a bi-manual assembly operation, and steadiness during aiming were measured. The effects of caloric restriction on two components ("travel" and "manipulation") of motion were examined using an electronic motion analyzer.[20] The task, involving the turning of a series of rotary switches, was performed under two conditions: a 10-minute period of continuous performance

at a "normal", "comfortable" speed, and a 2-minute period of performance at the maximum pace.

After more than three weeks on the experimental diet, the alterations in motor functions were surprisingly few and small. Changes in grip strength were negligible and neither the mean decrement during restriction nor the increment during recovery reached statistical significance. The lengthening of the time of the upward leg movement, indicative of a deterioration in performance capacity, was small in absolute terms but the individual alterations in the direction of deterioration were consistent and, consequently, the mean change statistically highly significant. The same was true of the reversal of the change during refeeding. In the test of finger dexterity (assembly of peg-washer-collar-washer units) there was no significant decrement in the number of units assembled per unit of time. Scores in the tests of steadiness showed no consistent trends.

In the motion-analysis test,[21] the mean time spent in the actual manipulation (turning) of switches, at either the "normal" or "maximal" pace, showed no substantial alterations. Statistically significant changes were limited to "travel" movements (from switch to switch).

In personality questionnaires the statistically significant changes were limited to the scales of the "psychoneurotic" triad (Hypochondriasis, Depression and Hysteria) of the Minnesota Multiphasic Personality Inventory. The magnitude of the shift (increment) in the means corresponded to about one standard deviation (Depression) or less.

The results, considered together with the biochemical and physiological data, indicate that men of good initial nutritional status and in good state of physical training, engaged in moderate amount of physical exertion in moderate climate, with free access to water, adequate salt intake and vitamin supplements, are able to subsist for 24 days without disabling alterations in performance capacity or morale on an all-carbohydrate diet of 1,000 calories per day.

5. PROLONGED CALORIC DEFICIT (SEMISTARVATION)

When the energetic equivalent of the food intake is lower than physiological requirements one speaks of calorie restriction. When the restriction is fairly severe and prolonged, it is referred to as "semistarvation."

In by-gone ages, the semistarvation of famines has been the most important nutritional deficiency facing mankind. There is no lack of incidental observations on the effects of brief but severe caloric restriction, characteristic of a variety of emergencies that have plagued travelers, explorers, sailors and soldiers. Still larger in extent and more ancient in origin are the reports about the effects of famine. World War II, with its concentration camps, besieged cities, and whole sections of widely separate countries subjected to famine, has contributed voluminously to this distressing chapter on human (or should it be "inhuman"?) nutrition. Much of the literature was summarized in connection with the presentation of experimental observations on semistarvation and nutritional rehabilitation, made at the University of Minnesota in 1944-45.[5]

Among the monographs on semistarvation published after 1950, the collaborative work by Danish authors should be noted.[22] During advanced stages of semistarvation the musculature becomes extremely atrophied. Loss of strength, muscular pains and cramps are prominent symptoms. The terminal phase is characterized by severe reduction of movements, including speech, and retardation of all mental processes.

Russian observations on semistarvation have been summarized.[23] In advanced stages of semistarvation, physical exertion leads rapidly to exhaustion which may pass into coma. The sensory thresholds are increased and pain sensitivity is diminished. The reaction of the pupils of the eye to light is weak. The activity of the sympathetic nervous system is decreased (lowered blood pressure, slow pulse) and the adrenals are atrophied. The extreme weakness is interpreted as a result of a complex of factors: decreased muscle mass, lack of energy yielding substances, and alterations in the activity of the motor nervous centers.

In regard to behavioral alterations, advanced semistarvation is characterized by sluggish intellective processes, decreased ability to concentrate, and incapacity for sustained mental effort. There is a lowering of all higher interests and feelings, and a tendency to daydream. Restlessness and irritability may alternate with periods of apathy, bordering on abulia. Some patients exhibit character disorders such as sullenness, obstinacy and lack of tact. Psychoses were rarely seen in patients with simple semistarvation, even at the height of the Leningrad famine. Hallucinations and other symptoms of psychotic disorders were present mostly in those patients in whom caloric deficit was complicated by pellagra, infection or trauma.

Experimental studies on semistarvation in man are difficult, in fact impossible except under very special circumstances. Such conditions — the combined availability of volunteers, funds, and research facilities — were present in 1944 and made possible the University of Minnesota study.[5] These investigations, although focussed on the evaluation of diets for nutritional rehabilitation (refeeding), yielded basic data on the effects of semistarvation in the absence of the factors typically complicating famines. In addition to the monograph[5] and the papers incorporated in it, communications were published dealing with the general picture of psychological changes in semistarvation and nutritional rehabilitation,[24] a pictorial test as a measure of frustration,[25] responses in the Rorschach inkblot test,[26] and a quantitative[27] and a qualitative[28] presentation of the case study of a typical subject.

In the course of 24 weeks the 32 subjects, initially normal young men who volunteered for the study as an alternative to military service for reasons of conscience, lost one-fourth of their pre-experimental body weight. Sensory functions[5b] were remarkably resistant to this severe nutritional stress. Visual thresholds remained unaltered. The acuity of hearing actually increased; this change, although small, was reversed in the course of nutritional rehabilitation and so probably represents a genuine, nutritionally induced alteration.

Clinical examinations of the neurological status yielded largely negative results. There was no impairment of the sense of vibration, tested by a tuning fork. Skin sensitivity remained normal, except for three men who developed sensory disturbances in the form of mild paresthesias. The patellar and the ankle tendon reflexes were diminished.

The components of the capacity for brief neuromuscular performance — strength, speed, and coordination — were examined by a battery of tests similar to those referred to in the section on acute starvation.[6] In semistarvation, changes in all of the psychomotor functions were statistically highly significant. However, there were substantial differences in the relative amount of deterioration. The largest decrement took place in the strength measurements in which the peripheral factors, the size and state of muscles, limited performance. The decrement in grip strength was 28% of the original value and in lift strength (measured by a back dynamometer) it was 30 per cent. Performances in which the central nervous system was the critical component, such as tapping and complex reaction time, changed but little. The average decrement in the speed of tapping amounted to 5%, the lengthening of the reaction time to 8% of the pre-starvation means. The pattern tracing, a complex task involving eye-hand (and foot) coordination and performed while the subjects were walking on a treadmill, was intermediary in regard to the relative amount of deterioration. The number of error contacts in the pattern tracing performances increased by 16 per cent.

It may be noted that the largest decrement took place in the endurance test which involved running on an inclined treadmill to exhaustion. The mean duration of the treadmill run decreased from 242 sec. to 50 sec., representing a decrement of about 80 per cent.

Measured intellective performance did not change importantly, in spite of subjective complaints about inability to concentrate and difficulty to maintain a trend of thought. Using "speed" tests of intelligence in which the working time was short and the performance strictly timed, no statistically significant decrement was obtained on tests of the perception of spatial relations, word fluency, short-term memory, inductive reasoning, and perceptual speed. In the "power" tests, with no rigid time limits imposed (the actual working times covered eight to ten hours spread over several test sessions), the total scores showed a minimal negligible decrement at the end of the semistarvation period. This was in marked contrast to the sharp decline in spontaneous mental effort and achievement which only gradually returned to "normal" upon refeeding. In the psychometric study of personality a variety of techniques was used. A marked rise was present in the "psychoneurotic" scales (Hypochondriasis, Depression, and Hysteria) of the Minnesota Multiphasic Personality Inventory. The mean change on the Depression scale was 20 units, i.e., 2 standard deviations (from 54 to 74, when "normal" mean = 50, 1 standard deviation = 10). In a group of 20 men re-examined 33 weeks after the end of the starvation period the mean score returned to the normal value of 51.

6. THIAMINE DEFICIENCY

Thiamine appeared to be the crucial factor in a study on the effects of a B-complex deficiency[29] in which motor[30] and intellective[31] functions, and personality[32] were investigated in substantial detail. The provision of supplementary thiamine was followed by a rapid return of the appetite and regression of other functional abnormalities. This was regarded as an indication that thiamine was the component accounting for the development of the early symptoms of B-complex deficiency. In the subsequent study the experimentally varied dietary component was limited to thiamine alone, with other dietary components provided in adequate amounts.

The experiment[33] consisted of 4 periods: (1) a month devoted to standardization and collection of control measurements; (2) 168 days of partial restriction of thiamine, with respective daily intakes of 0.6 (four men, basal diet), 1.0 (four men, thiamine supplement of 0.4 mg/day) and 1.8 mg (2 men, thiamine supplement of 1.2 mg), at the energy expenditure of about 3,300 calories; (3) a period of acute thiamine deprivation lasting 15 to 27 days (depending on individual rates of development of deficiency symptoms), during which all 10 men received a thiamine-free diet with no thiamine supplements; and (4) a 9 to 21 day period of a thiamine-free diet supplemented with 5 mg thiamine daily.

During the standardization period, all subjects were maintained on an adequate diet, identical in composition. They became thoroughly familiar with a wide variety of physiological and psychological test procedures. In those areas, such as intellective and motor functions, in which practice affects test scores, determined effort was made to reach stable plateaus. The measurements obtained at the end of the standardization period represented the "normal", control values.

Here we shall focus on the data obtained in the period of acute thiamine deprivation, during which the subjects received a diet essentially free of thiamine, but adequate in all other respects. The data will be considered for the group of ten men as a whole; it should be noted, however, that differences in the thiamine intake during the preceding period of partial restriction were reflected in the magnitude and, more importantly, the time of the onset of physiological and behavioral deficiency symptoms. Oral administration of thiamine was started for each man when the deficiency had progressed as far as was considered safe.

At this time general weakness and incoordination of the legs were very pronounced, anorexia was extreme, and the level of plasma pyruvate was elevated. On the tenth day of acute thiamine deprivation, the average plasma pyruvate levels, measured one hour after oral administration of 100 gm of glucose, were 2.0, 1.5 and 1.3 mg per ml in the groups previously maintained on supplements of 0, 0.4, and 1.2 mg of thiamine per day.[34]

In these groups vomiting first occurred on the 5th, 14th and 22nd day, respectively. It was preceded by anorexia and nausea, the first functional signs of thiamine deficiency. Neuropsychiatric findings (weakness in the legs, paresthesias, nerve trunk and muscle tenderness) were especially frequent and marked in the group that received no supplement during the prolonged period of partial re-

striction. In one of the four men in this group the muscle weakness and poor coordination reached such a degree that he was unable to stand up from a squatting position without help. These symptoms, including peripheral nerve involvement, indicated that the thiamine deprivation resulted in an incipient beri-beri.

Semi-quantitative self-ratings, based on symptoms of "neurasthenia", indicated a marked deterioration during thiamine deprivation, followed by a rapid and remarkable recovery in the course of thiamine supplementation. The signs of peripheral neuropathy were more refractory. In one man definite residues, in the form of a peculiar gait, remained for several months.

Large changes in the direction of deterioration were observed during thiamine deprivation on the "psychoneurotic" scales of the Minnesota Multiphasic Personality Inventory, with a maximum on the "Depression" scale. On a scale with normal mean = 50 and standard deviation = 10, the mean score at the end of thiamine deprivation was 82, three standard deviations above the "normal" mean. These are the changes for the groups of all ten men. In the sub-group that received no supplements to the basal diet during partial restriction, the mean at the end of acute deprivation reached the startling value of 93 and returned to the normal value of 54 upon thiamine supplementation.

Within the limits of experimental conditions, intelligence test performance was not affected adversely by the total, but relatively brief, thiamine deprivation. Measured intellective functions remained surprisingly stable and free from deterioration both when long or brief tests were used.

There were only marginal decrements (slowing down) on tests of central nervous functions involving the perception of a rapid sequence of light flashes (critical fusion frequency) and fluctuations of perspective of an ambiguous cube. Neither auditory acuity, measured for three frequency levels of the stimulus, nor the vibratory sensitivity measured at the ankle bone, were affected. The elevation of the vibration threshold determined at the sole of the foot is of questionable significance. In the area of sensory functions the most consistent change was observed in the pressure-pain threshold. A statistically significant decrement (increased sensitivity) occurred during thiamine deprivation with a return toward "normal" on supplementation.

As regards motor functions, the changes in eye-hand coordination during movement (pattern-tracing) and in manual steadiness were in the direction of deterioration and there was significant improvement on thiamine supplementation. Body sway, although individual responses were highly variable, increased during acute thiamine deprivation and was reduced during recovery. Analysis of records of eye movements during reading disclosed no consistent changes.

There was a definite deterioration in speed of motion, whether the motion involved repetitive movements of the upper arm and hand (test of manual speed and coordination) or two types of tests of reaction time. In the test of two-plate tapping the change in thiamine deprivation was also in the direction of

deterioration but only the recovery upon thiamine supplementation was significant statistically.

Surprisingly enough, the results of strength tests (grip strength, lift strength) indicated only negligible changes.

The significance of this study is, partially, its contribution to available information on thiamine requirements of normal young men and the amount of protection afforded during a period of deprivation by previous level of thiamine intake. The men maintained on the highest intake (1.8 mg/day) during partial restriction were able to withstand the subsequent thiamine deprivation longer (27 days) than the men on the lowest thiamine intake (0.6 mg/day) who developed disabling symptoms within 19 days, on the average. The men on the intermediary intake (1.2 mg/day were also intermediate in reference to the resistance to thiamine deprivation but were closer to the high-thiamine group (26 days). The course of the deficiency symptoms was much the same for all the subjects.

While these details are of interest, the principal merit of this work is the comprehensive quantitative characterization of the psychological changes produced by acute thiamine deprivation and reversed by means of thiamine supplements. The effects of supplementation were dramatic both in the speed and degree of recovery.

7. CLINICAL AND FIELD STUDIES

The present review is limited essentially to experimental investigations but it may not be out of place to refer briefly to some facts and activities in the clinical segment of research on the impact of nutrition on behavior. Deficiency of all of the major nutrients, including water,[2] eventually affects behavior even though the mechanisms involved will vary. There may be a general debility (as in severe semistarvation), muscular dystrophy (caused in the rat by the lack of vitamin E), mechanical damage to nervous tissues (in pups deficient in vitamin A), or impairment of nervous function, central and peripheral, through interference with neural metabolism. This may result from an inadequate supply of critical nutrients (loss of consciousness resulting from low blood sugar) or from impaired utilization of food stuffs (thiamine deficiency).

Nutritional deficiency of nicotinic acid may result in a genuine psychosis. The treatment of the dementia of pellagra offers a unique, so far scientifically not fully exploited opportunity for the application of psychometric tools in nutritional research. In experimental, metabolically oriented studies on induced niacin deficiency,[35] depression and apathy were noted as part of the deficiency syndrome, in the absence of demonstrable neurological changes, but no quantification of the behavioral changes was attempted.

Similarly, no quantitative data on emotional, intellective or psychomotor characteristics were obtained in experimental studies on pantothenic deficiency.[36] The syndrome, induced by maintaining initially normal volunteers on a diet devoid of pantothenic acid or containing a metabolic antagonist (omegamethyl panto-

thenic acid), included such behavioral and sensory changes as profound apathy and depression, neuromotor disorders with paresthesias (numbness and tingling in the extremities, burning sensations in the feet) and complaints of clumsiness, dizziness and weakness. The men, cheerful at the outset, became quarrelsome, sullen and petulant. The symptoms were reproduced on extending the observations to additional subjects.[37]

Behavioral changes associated with severe protein malnutrition in children (kwashiorkor) have been studied in Kampala, Uganda.[38] The behavior at three stages of recovery was described qualitatively and in reference to results obtained on standardized tests of psychomotor development.

In phenylpyruvic oligophrenia, a rare form of mental deficiency, we encounter not a dietary deficiency but rather a faulty protein metabolism. Specifically, the "inborn error of metabolism" is manifested as a failure to metabolize normally phenylalanine, a dietary amino acid. An excess of phenylalanine accumulates in body fluids. In part, the substance is converted into phenylpyruvic acid which the patients are also unable to oxidize and which they excrete in the urine.[39] By maintaining children with phenylpyruvic oligophrenia on diets low in phenylalanine, substantial improvement in mental functioning has been reported.[40, 41, 42] For a time, the matter appeared simple, with the mental deficiency regarded as a direct result of the damage to the central nervous system, brought about by the accumulation of phenylalanine and of its breakdown products in body fluids and tissues. It appears that the excretion of phenylpyruvic acid in the urine is not unconditionally associated with mental deficiency. Thus, the real cause of mental impairment in patients with phenylketonuria remains yet to be specified.

Glutamic acid is also an amino acid. For a period of time it was the most actively investigated topic in the border area between psychodietetics and psychopharmacology. It was studied in reference to the prevention of convulsions, restoration of consciousness in hypoglycemic subjects, and treatment of mental deficiency.[43] Psychometric methods were used in numerous studies carried on with mentally defective subjects, with equivocal results as far as the effectiveness of the treatment is concerned.

Glutamic acid and its amid are substances appearing in high concentration in the central nervous system. Glutamic acid can serve as a substrate for oxidative processes in nerve tissues under conditions of insufficient glucose supply. Nutritionally, glutamic acid is classified as a non-essential amino acid, readily synthesized in mammalian organisms. Furthermore, it is contained in substantial amounts in animal and vegetable proteins. In the majority of clinical studies on the effects of glutamic acid administration, little or no attention has been paid to the amount of glutamic acid provided in the diet. Patients given supplements of glutamic acid are expected, then, to benefit from limited amounts of a substance which is already provided, in relatively large quantities, in the dietary proteins.

It is perhaps not surprising, under these conditions, that well-controlled studies on the effects of glutamic acid on intelligence tend to yield negative

results. The mechanism of improvements, beyond the range of random fluctuations, reported in some studies is uncertain. The measured intellectual gain may represent a real improvement in intelligence or a better, more effective utilization of existing intellectual abilities through improved emotional control. The second alternative appears to be more likely.[44] A valid appraisal of the practical significance of glutamic acid supplementation will require a more precise differentiation of the types of mental deficiency, based on a better knowledge of their etiology. It is clear that glutamic acid supplementation would not be a rational therapy for patients with phenylpyruvic oligophrenia.

Among the trace minerals, iodine is of special interest. Deficiency of iodine depresses the hormonal output of the thyroid gland which controls the rate of energy metabolism (cellular oxidation) and influences physical growth and neuromuscular functioning. Severe hypothyroidism present in childhood results in cretinism, a condition which tends to be associated with retarded mental development in the young, and with dullness and apathy in the adult.[45] These facts are well known. However, there is place for field research using standardized psychometric tools and directed toward the elucidation of the role of iodine intake and production of thyroid hormone in mental development. Neurophysiologically, the depressed function of the central nervous system in a hypothyroid condition is manifested in the impaired ability to form conditioned reflexes.

8. ANIMAL BEHAVIOR

Partly because of limitations of space, this review was focused on experiments with man. This should not be interpreted as a disdain for animal experimentation. Rigorously controlled experimental studies on the effects of nutritional deficiencies in human beings are difficult, at best, on account of the heavy demands on the time of both the subjects and the experimenters as well as other considerations.

Interestingly enough, one set of roots of the research on diet and the functioning of the central nervous system, characterized in terms of the formation and maintenance of conditioned responses, goes to the Laboratory of I. P. Pavlov. The studies were carried out on dogs by two of Pavlov's students.[46, 47] The experiments were designed not by the experimenters but by the stark fact that, following World War I, the food supplies in Leningrad became grossly inadequate. As in other dietary stresses,[48] one of the earliest neurophysiological symptoms of semistarvation was the loss of differential inhibition. Differential inhibition refers to the animal's acquired ability to restrict conditioned responses to stimuli made initially effective through repeated reinforcements, and not to respond to quite similar but, normally, distinguishable stimuli, regularly nonreinforced. In the next stage of semistarvation, well established conditioned responses, elicited under standard conditions, decreased in intensity. The reactivity of the central nervous system was lowered and it became impossible to elaborate new conditioned responses. In time, responses to previously conditioned artificial stimuli, such as the sound of a bell, decreased and finally could no longer be elicited. However, the responses to natural conditioned stimuli, such

as the sight or odor of food, were still retained in considerable force. In the terminal phase of semistarvation even these responses were greatly reduced. The unconditioned salivary reflex, elicited by a direct contact of the mouth with food, continued to function throughout, although the intensity of the reflex was depressed.

In addition to the acquisition of conditioned responses, American investigators studied various other aspects of animal behavior in reference to nutrition, including learning (using dry and water mazes) and problem solving, general activity as measured by the revolving drum technique, endurance in swimming, and dark adaptation.[8b] Swimming and running were considered as the most promising methods for measuring physical performance capacity in connection with the evaluation of army rations by animal experiments;[49] the authors recognized the value of test situations involving maximal stresses as well as performance of submaximal work sustained for prolonged periods.

In a study on the effects of starvation, superimposed on pantothenic acid deficiency, a modification of the "Skinner box" was used.[50] Rats, placed in low-temperature environment, learned to activate a heat lamp. The experimental animals showed a more marked increase in the frequency of lever-pressing than the controls. It was concluded that the animals deprived of both pantothenic acid and of food were more sensitive to cold than the animals deprived only of food.

The "operant conditioning" apparatus and methods were adapted also to refined measurement of food intake in the mouse.[51, 52] Both the number of food pellets released and the time of the delivery of each pellet are recorded.

9. DIET AND BEHAVIOR — A PROSPECT

Studies on the impact of deficient diet on behavior require competence and facilities for the handling of both sides of the equation, i.e., of diet *and* behavior. Ideally, such studies should be an interdisciplinary enterprise.

Apparently the only research establishment devoted specifically to the study of these problems — be their methods and their choice of subjects limited — is the Laboratory of Higher Nervous Activity, under Prof. A. I. Makarychev. The Laboratory is a subdivision of the Institute of Nutrition, in Moscow, headed by Prof. O. P. Molchanova, a unit in the Academy of Medical Sciences, U.S.S.R.

The area of studies on the impact of diet on behavior is a part of the larger field of "psychochemistry." At present, psychopharmacology dominates the scene. It is likely that the methodology developed in the context of studies on drug effects will enrich the researches on diet and behavior.

Another facet of psychochemistry involves the correlation between biochemical characteristics of the brain, with emphasis on the enzymes (specifically, the cholinesterase), and the individual differences in behavior within the limits of normality.[53] Cholinesterase activity is considered as an indicator of acetylcholine metabolism. It is a stable characteristic, reliably differing among individuals, and the enzyme is known to be involved significantly in normal neural and inter-

neural functioning. The results indicate the presence of a correlation between the individual differences in the activity of this brain enzyme and the individual differences in adaptive behavior as measured by performance on certain maze tests. The studies are being extended to other types of adaptive behavior and other brain enzymes. Experimentally, the authors approach the problem genetically, by breeding animals (rats) selectively for specific brain chemistry and then testing for behavioral effects. While the science of nutrition is principally concerned with the biochemical bases of the *changes* in behavior effected in a given organism by varying the dietary intake, information on enzymic activity and behavior is of definite interest and relevance.

A systematic review of abnormalities of neural function in the presence of inadequate nutrition is in press.[54] In addition to the topics discussed, the effects of deficiency of vitamins (A, riboflavin, niacin, pantothenic acid, pyridoxine, B_{12}, E), protein, minerals (sodium chloride, calcium, manganese, iodine, cobalt, copper) and water are considered taking into account the relevant neurophysiological and clinical observations. Furthermore, the presentation is not limited to alterations in nervous function resulting from nutritional deficiencies but encompasses also the non-deficitary abnormalities, nutritional in origin, such as the spastic paralysis (lathyrism) which develops in individuals consuming large amounts of lathyrus peas. The neurological and behavioral manifestations induced by the ingestion of some species of mushrooms may also claim the right to be considered as a topic in "psychodietetics."

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